

Illumina's assays do *not* indicate the relative strength of binding

Court's Construction

12. The phrase "indicating an extent of hybridization," as used in the claims of U.S. Patent No. 5,795,716, means "indicating the relative strength of binding."

'716 Patent Claim 1

What is claimed is:

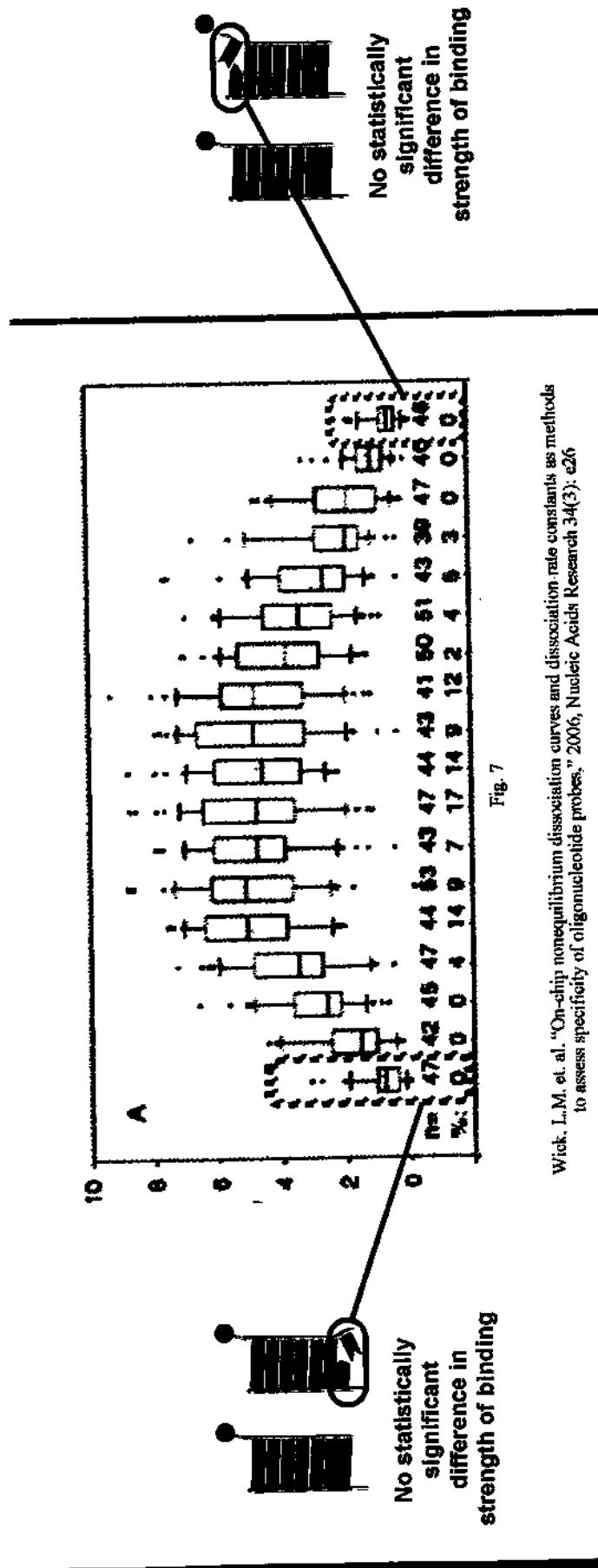
1. A computer program product that identifies an unknown base in a sample nucleic acid sequence, comprising:
computer code that receives a plurality of signals corresponding to probe intensities for a plurality of nucleic acid probes, each probe intensity indicating an extent of hybridization of a nucleic acid probe with at least one nucleic acid sequence including said sample sequence, and each nucleic acid probe differing from each other by at least a single base;
computer code that performs a comparison of said plurality of probe intensities to each other;
computer code that generates a base call identifying said unknown base according to results of said comparison and said sequences of said nucleic acid probes; and
a computer readable medium that stores said computer codes.

- Illumina's assays — perfect match and mismatch have *indistinguishable* strength of binding

- Illumina's assay intensities indicate the extent of enzymatic reaction, *not* relative strength of binding

Markman Order at ¶12

End-base mismatches do *not* typically show different strength in binding



- Conditions must be optimized to detect any difference in strength of binding
- End mismatch has little to no effect on strength of binding, even for short probes
- Illumina's assays are designed to do the opposite — longer probes and conditions set to avoid any differences in strength of binding

GoldenGate intensities do not "indicate an extent of hybridization" as required by claim 1

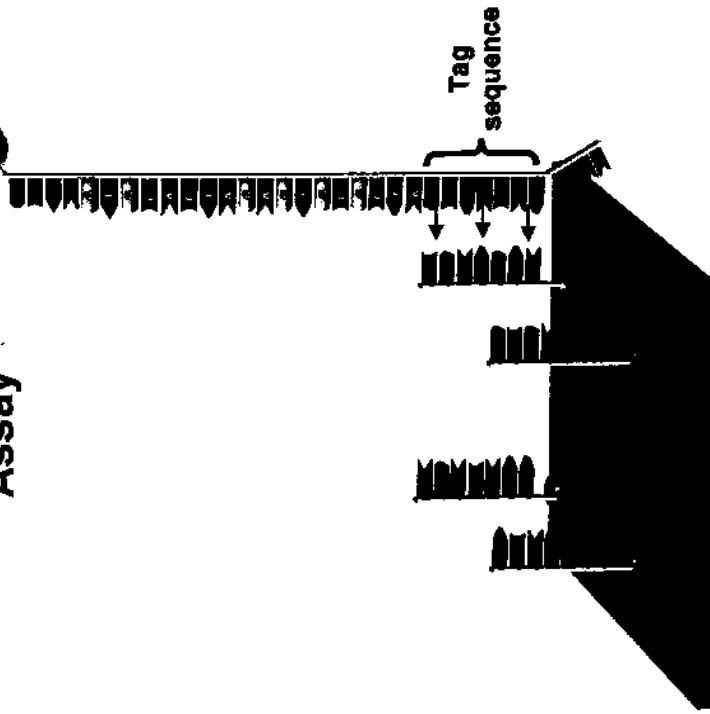
'716 Patent Claim 1

What is claimed is:

1. A computer program product that identifies an unknown base in a sample nucleic acid sequence, comprising:

computer code that receives a plurality of signals corresponding to probe intensities for a plurality of nucleic acid probes, each probe intensity indicating an extent of hybridization of a nucleic acid probe with at least one nucleic acid sequence including said sample sequence, and each nucleic acid probe differing from each other by at least a single base; computer code that performs a comparison of said plurality of probe intensities to each other; computer code that generates a base call identifying said unknown base according to results of said comparison and said sequences of said nucleic acid probes; and a computer readable medium that stores said computer codes.

GoldenGate Assay



Tag has exact same sequence for match or mismatch (i.e., no difference in strength of binding)

'716 Patent col. 41:59-67; 42:58-67

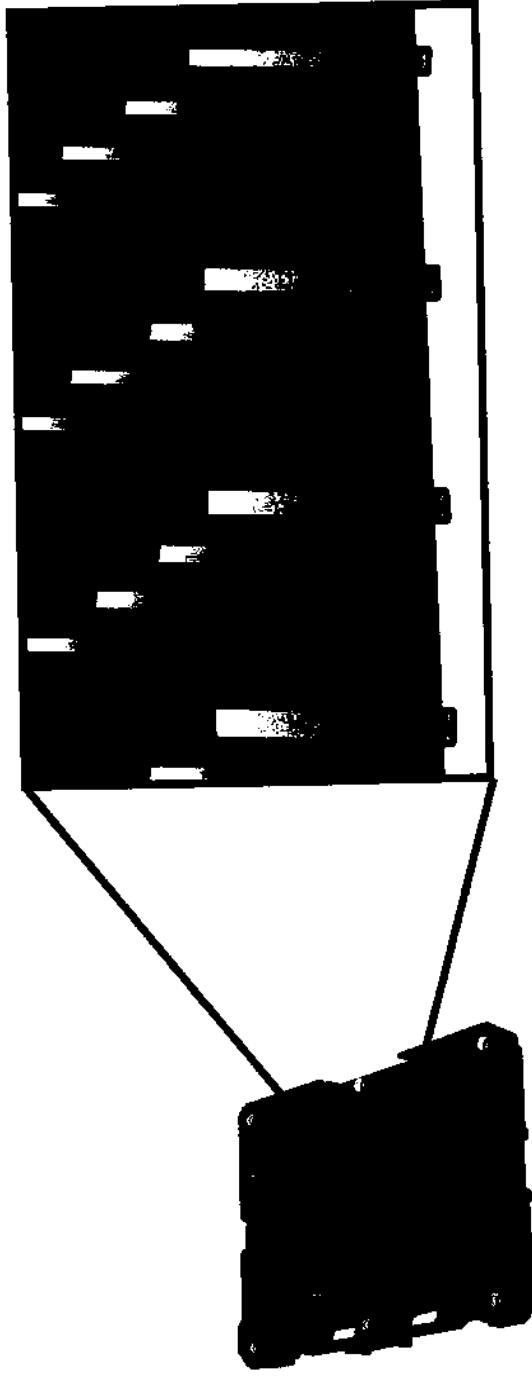
Array Matrix Not A "Biological Chip Plate"

'531 Patent Specification

G. Biological Chip Plate: A device having an array of biological chips in which the probe array of each chip is separated from the probe array of other chips by a physical barrier resistant to the passage of liquids and forming an area or space, referred to as a "test well," capable of containing liquids in contact with the probe array.

'531 Patent col. 4:19-25

**NO separate
"biological chips"
on a plate**



Array Matrix
underside

BeadChip Not A "Biological Chip Plate"

'531 Patent Specification

G. Biological Chip Plate: A device having an array of biological chips in which the probe array of each chip is separated from the probe array of other chips by a physical barrier resistant to the passage of liquids and forming an area or space, referred to as a "test well," capable of containing liquids in contact with the probe array.

'531 Patent col. 4:19-26



**NO separate
"biological chips"
on a plate**

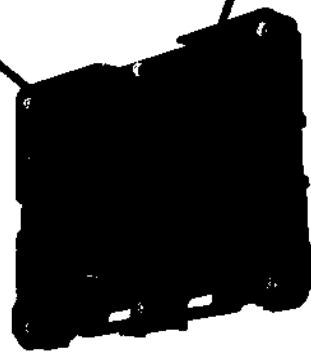
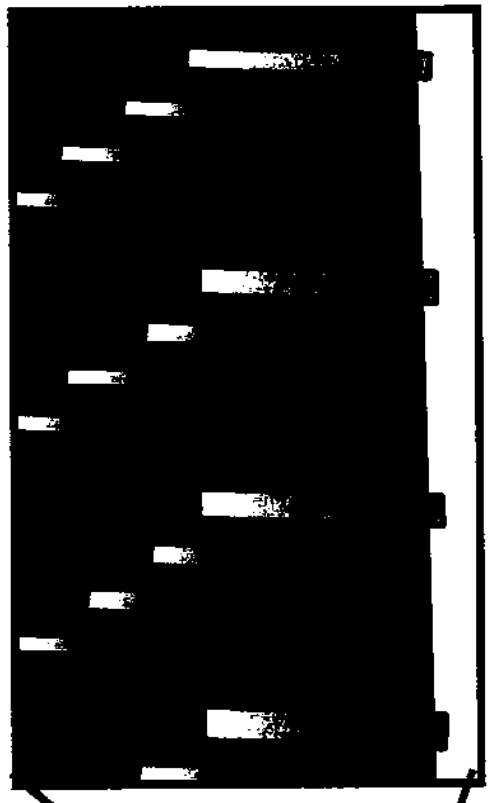
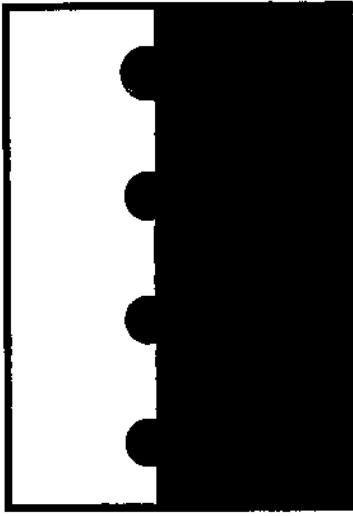
Illumina's Array Matrix Does Not Have A "Wafer"

'531 Patent, Claim 1

1. A method for making a biological chip plate comprising the steps of:

(b) providing a wafer comprising on its surface a plurality of probe arrays, each probe array comprising a collection of probes, at least two of which are different, arranged in a spatially defined and physically addressable manner;

Claim 1, '531 Patent, col. 12:41-49



Array Matrix
topside

Array Matrix
underside

Illumina's Products Do Not Meet The Attaching Step According To Affymetrix's Own Expert

Affymetrix's Expert Report

43. Additionally, neither of the Chetverin references describes a method for "attaching the wafer to the body so that the probe arrays are exposed to the spaces of the wells," as required by claims 1 and 2 or "applying a material resistant to the flow of the liquid sample so as to surround the probe arrays, thereby creating test wells" as required by claims 3 and 4.
Felder Report at ¶ 43

Chetverin '463 Patent

The sectioned array can also be created by applying a lattice to the solid support and bonding it to the surface so that each area is surrounded by impermeable walls. The technique of application of the lattice to the support is not critical; such means are well known in the art and include using adhesives and heat bonding.

'463 Patent at col. 10:28-34

Illumina's Products -- NO "attaching"

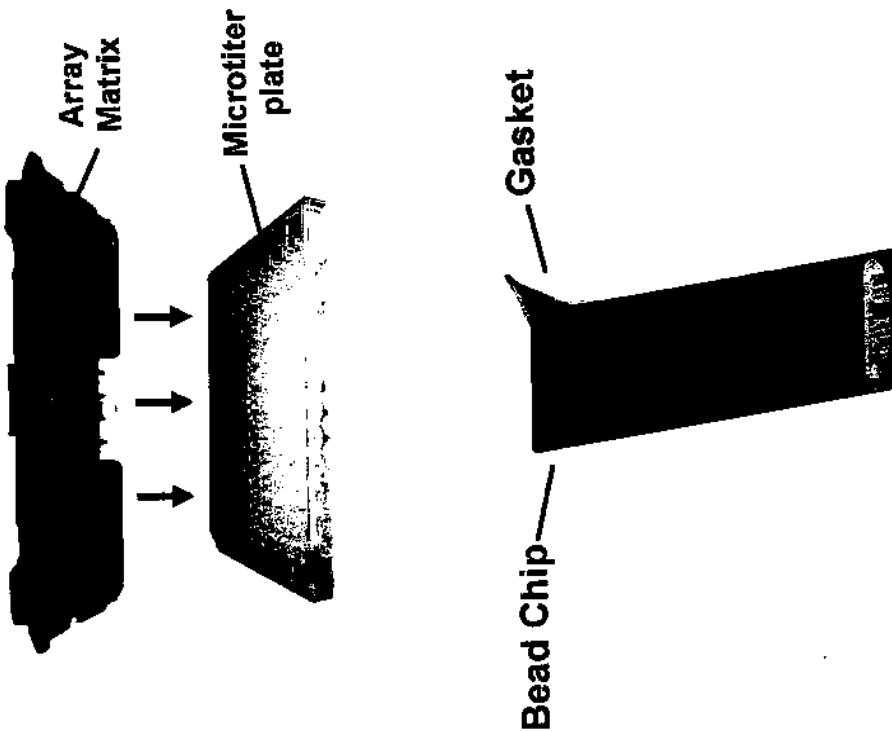
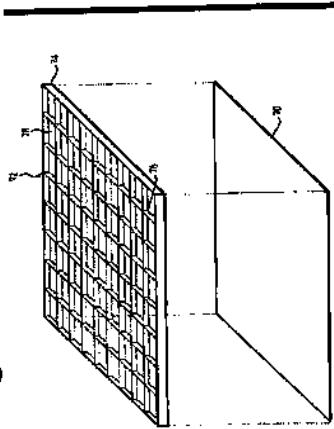
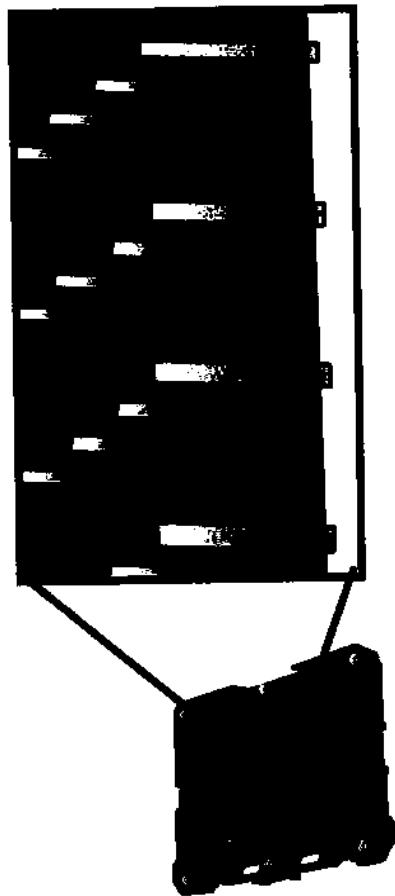


Fig. 3 of '463 Patent



Illumina Does Not Infringe The '531 Patent

- Not a biological chip plate



Array Matrix underside

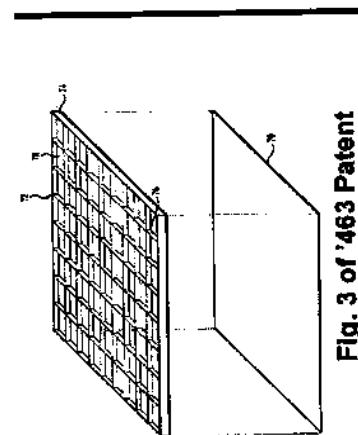


Fig. 3 of '463 Patent

- No attachment of accused "wafer" to body by Affymetrix's own expert

“Encoding System” As Defined By The Court

IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE

AFYMETRIX, INC.,
Plaintiff,
v.
ILLUMINA, INC.,
Defendant.

Civil Action No. 04-901 JJP

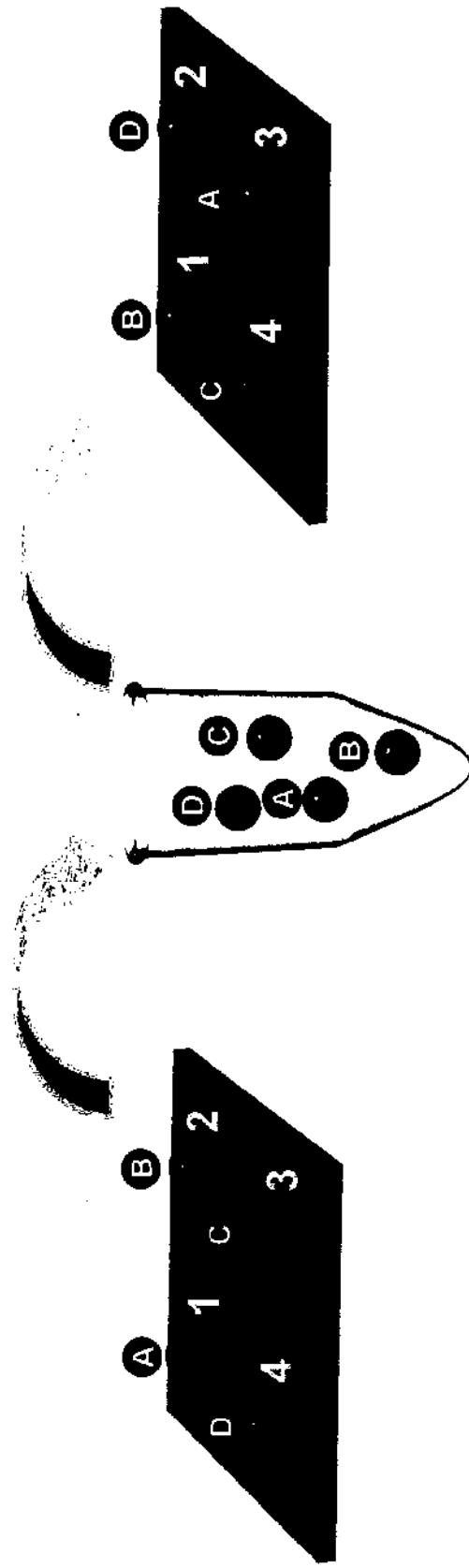
D.D.S.A.

1. The phrase “**said beads being coded with an encoding system**,” as used in the claims of U.S. Patent No. 6,355,432, means “**said beads having a property associated with each bead** [REDACTED] that can be used to distinguish one bead from another;”
2. The term “**target specific sequence**,” as used in the claims of U.S. Patent No. 6,355,432, means “**a known polymer sequence that has affinity for another sequence**.”
3. The term “**substrate**,” as used in the claims of U.S. Patent No. 6,646,243, means “**a material having a rigid or semi-rigid surface**.”

property associated with the bead

separate from the binding polymer

The Accused Spatial Location "Map" Is Not A Property Of The Bead



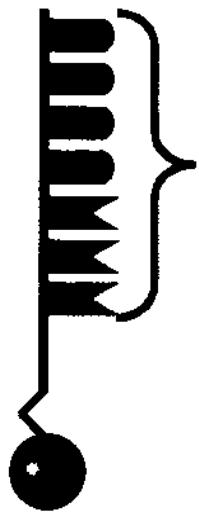
Location	
Bead	Location
A	3
B	1
C	4
D	2

Location	
Bead	Location
A	1
B	2
C	3
D	4

Location is not constant

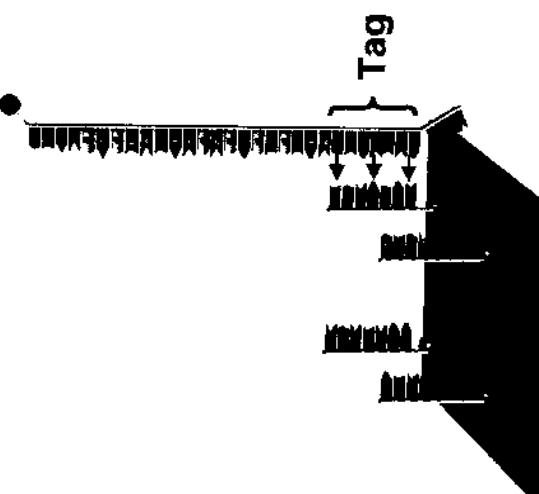
Illumina's Beads Have No "Encoding System" Separate From The Binding Polymer

- **Golden Gate/DASL bead address is NOT separate from the binding polymer**



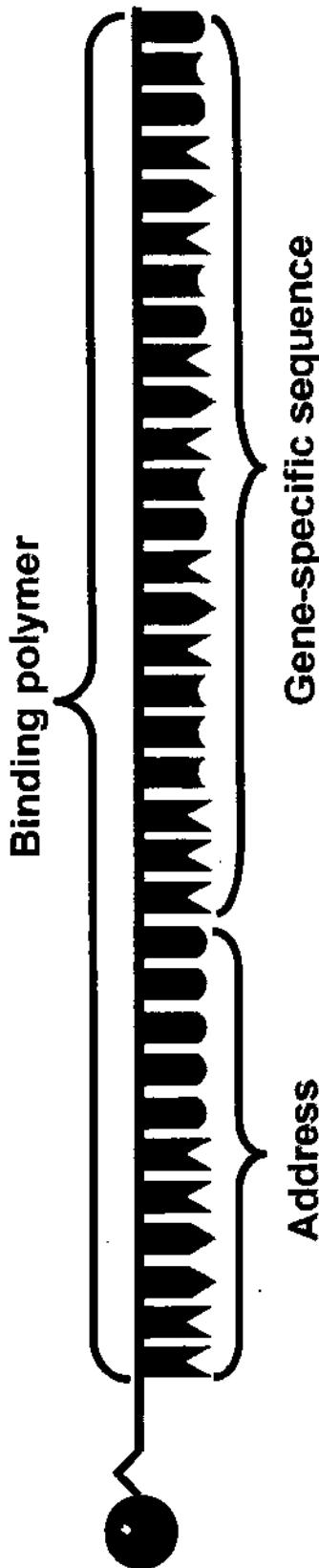
- **Address has two functions:**

- 1) capture assay products
- 2) used to decode array in manufacturing



Illumina's Beads Have No "Encoding System" Separate From The Binding Polymer

Infinium/Direct Hyb bead **address** is **part of** the binding polymer, **NOT** separate from it

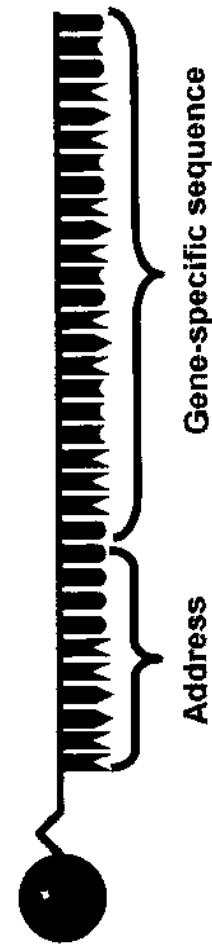


DNA on bead serves two functions:

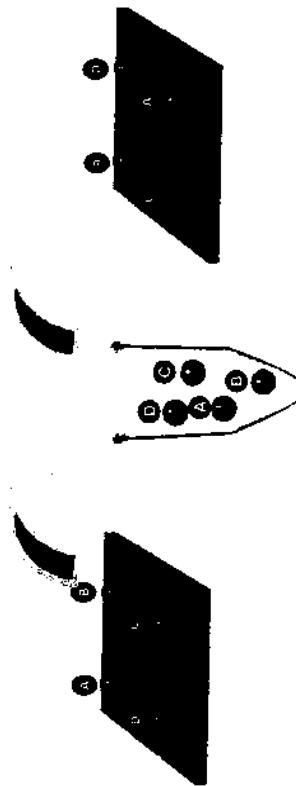
- **capture gene-specific sequences**
- **used for decoding in manufacturing**

'432 Patent Claims 2 And 9 Not Infringed Because No "Encoding System"

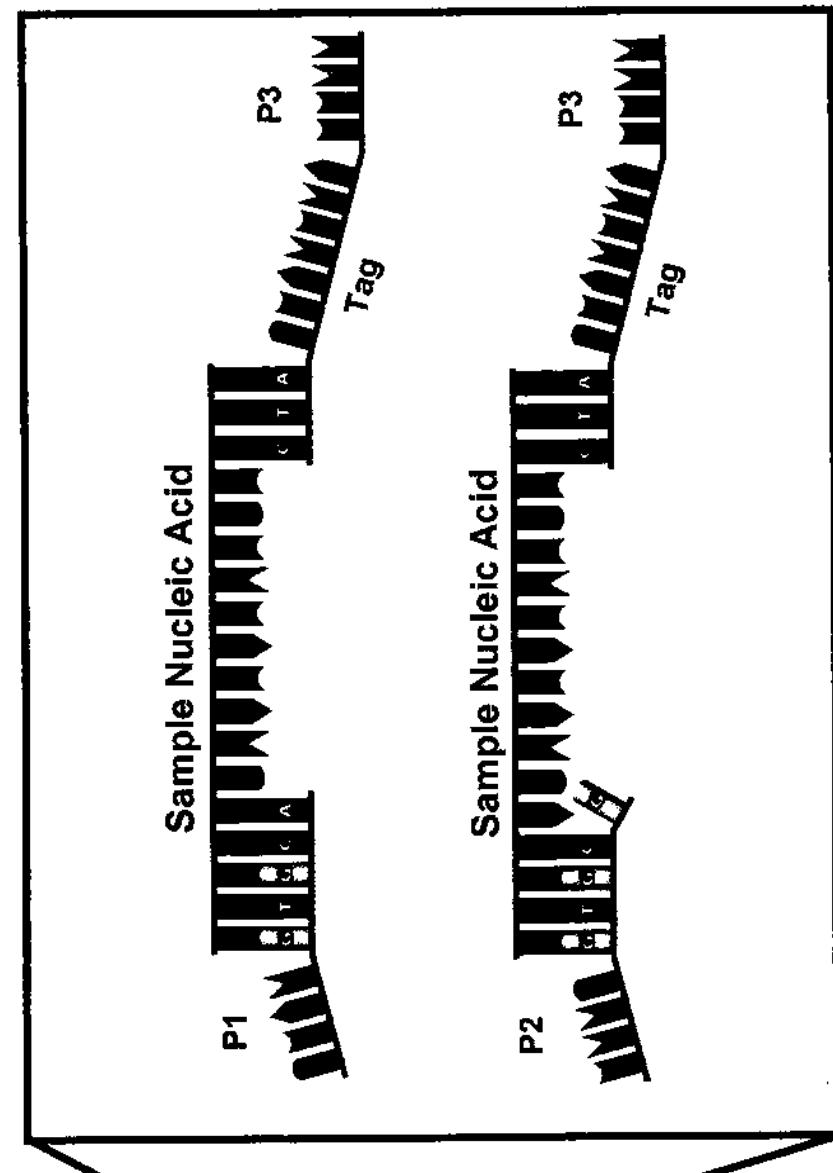
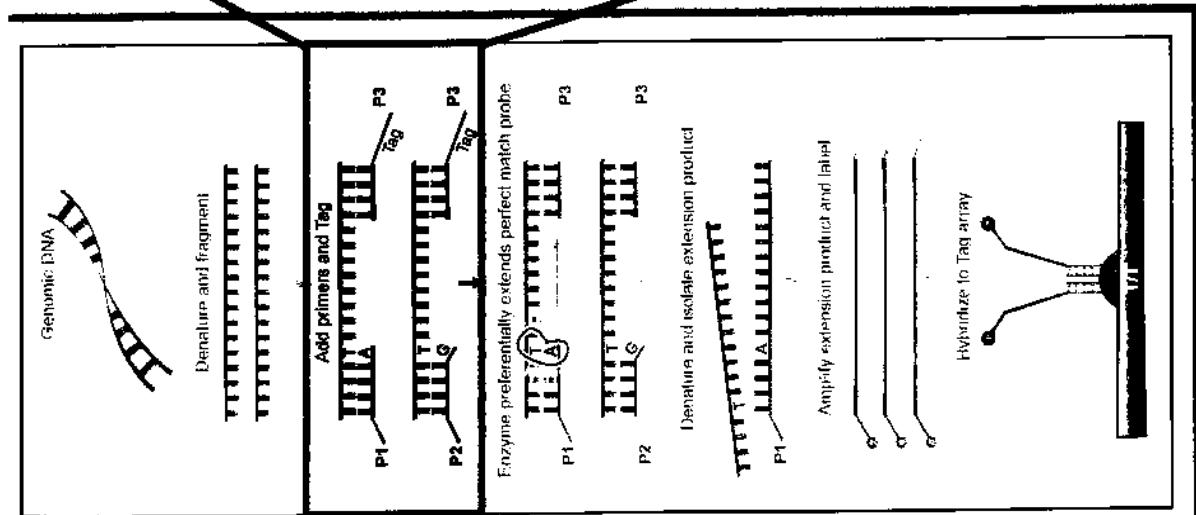
- Address of the Infinium/
Direct Hyb assay beads
are not separate from
binding polymer



- Spatial location is **NOT a property associated with each bead** so it is not an "encoding system" under the Court's construction

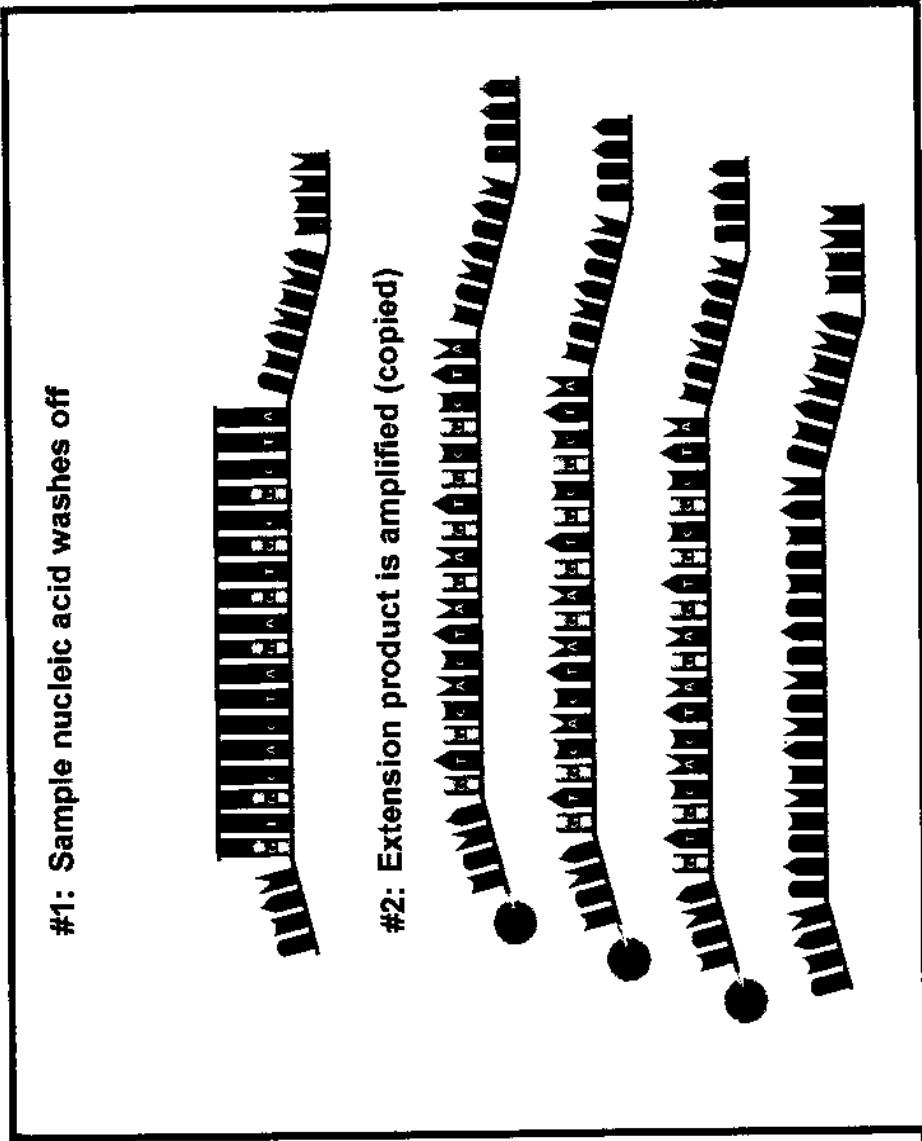
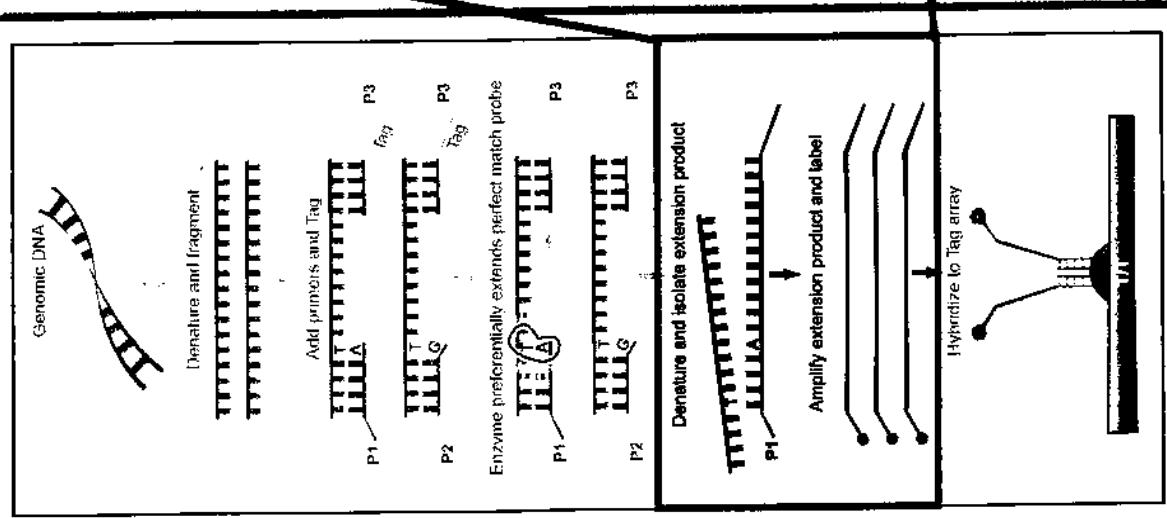


Illumina's GoldenGate Assay: Step 1



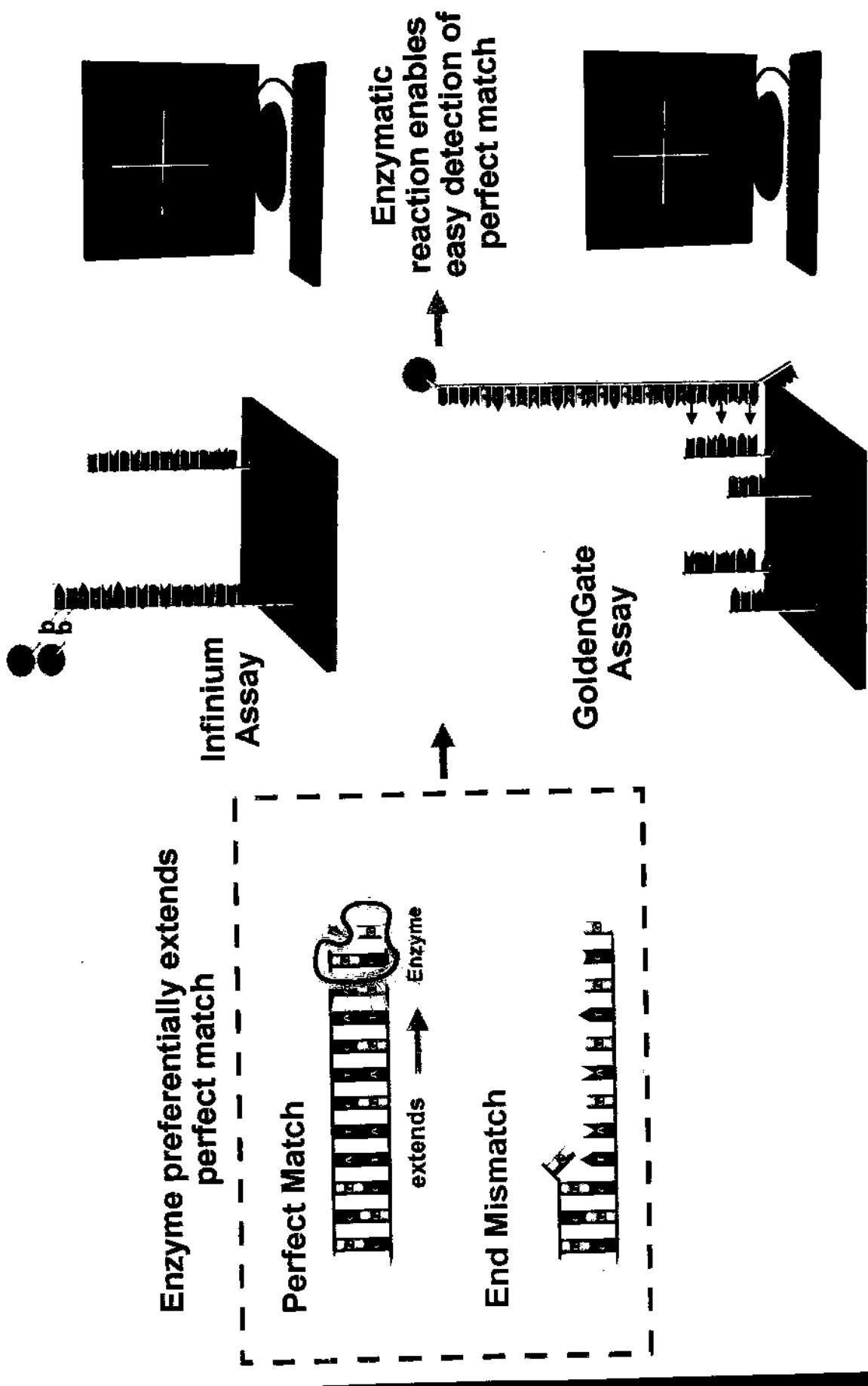
- Probes with P1 & P2 added to bind with sample nucleic acid adjacent to unknown base
- Locus specific nucleic acid with Tag sequence and P3 binds to downstream part of sample nucleic acid

Illumina's GoldenGate Assay: Step 3



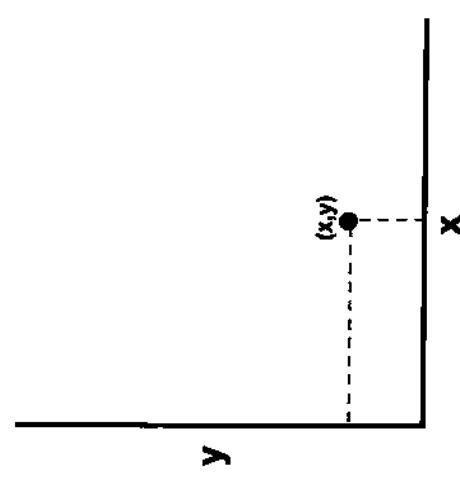
- Sample nucleic acid is separated from extension product and washed off
- Extension product is amplified (copied) and labeled

Illumina's Enzyme-Based Assays

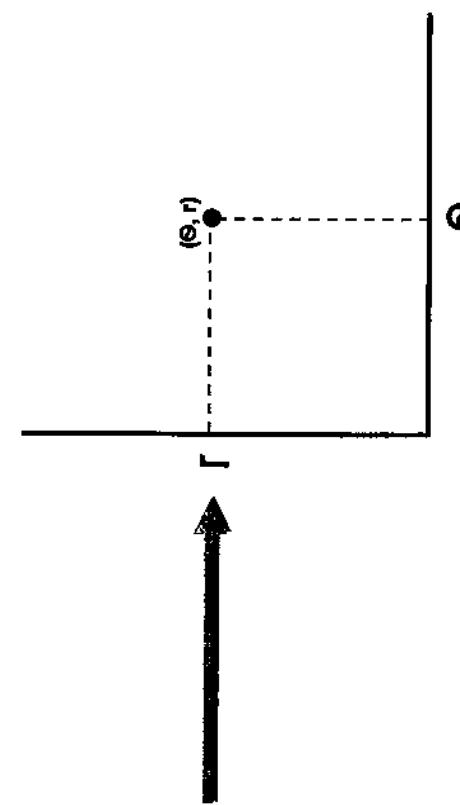


GenCall Polar Transformation: Like Transforming Your Address Into Latitude/Longitude

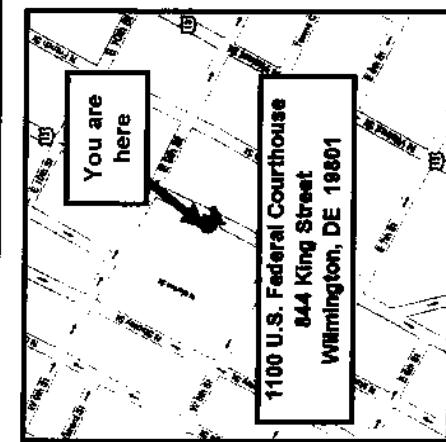
GENCALL CARTESIAN GRAPH



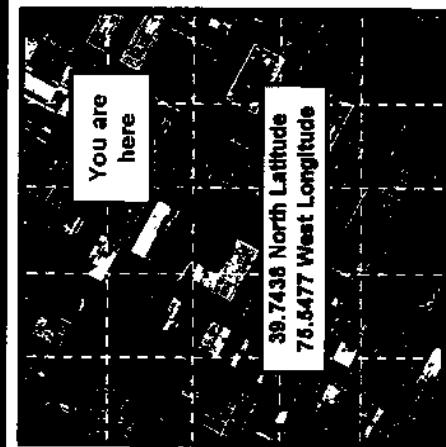
GENCALL POLAR GRAPH



DOWNTOWN WILMINGTON, DE



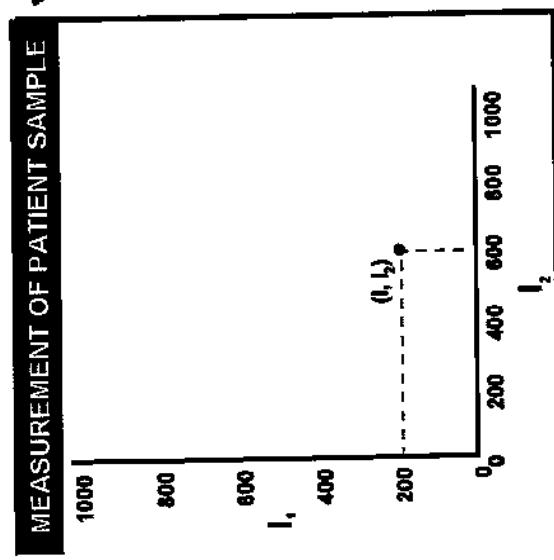
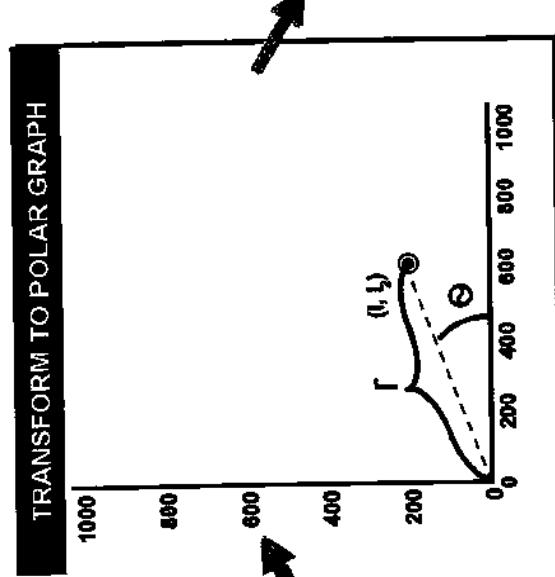
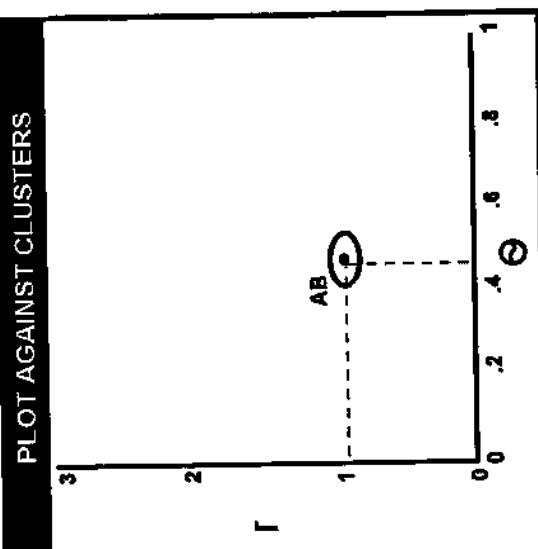
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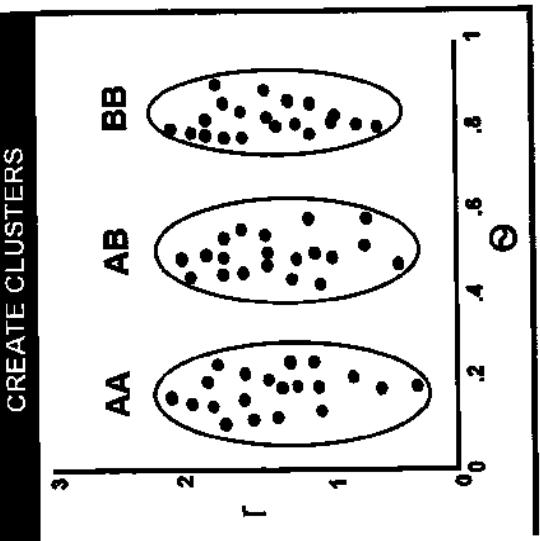
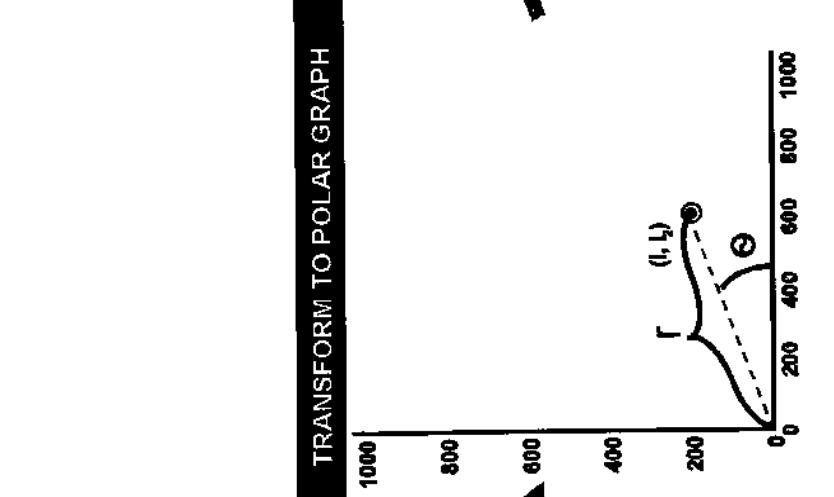
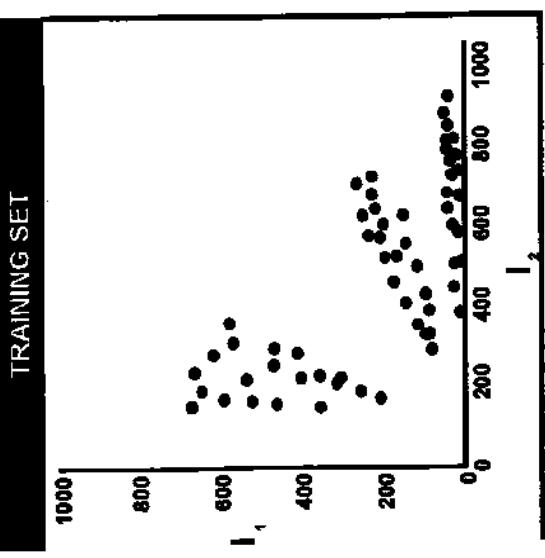
Longitude

Latitude

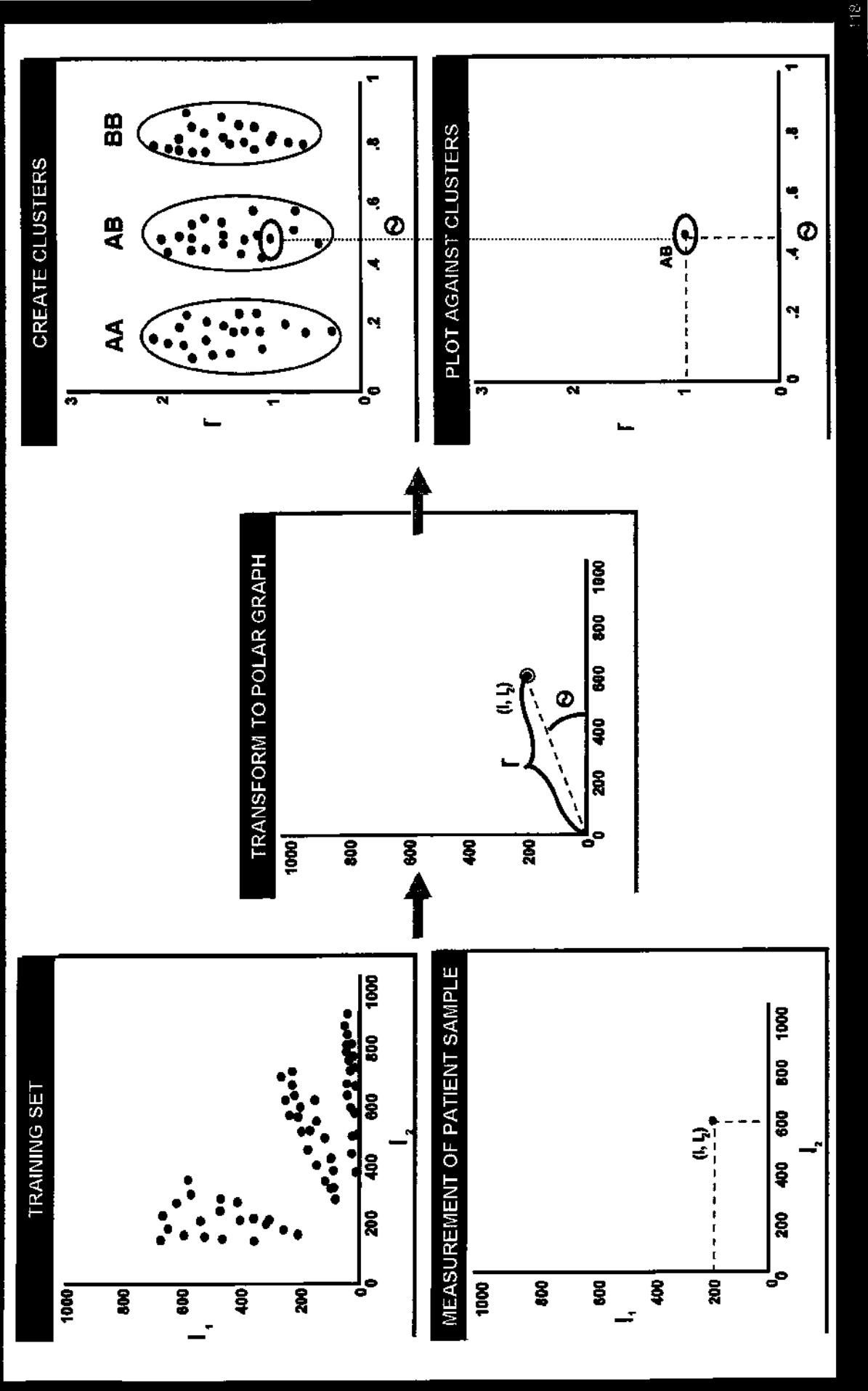
Illumina makes genotyping calls through transformation and clustering



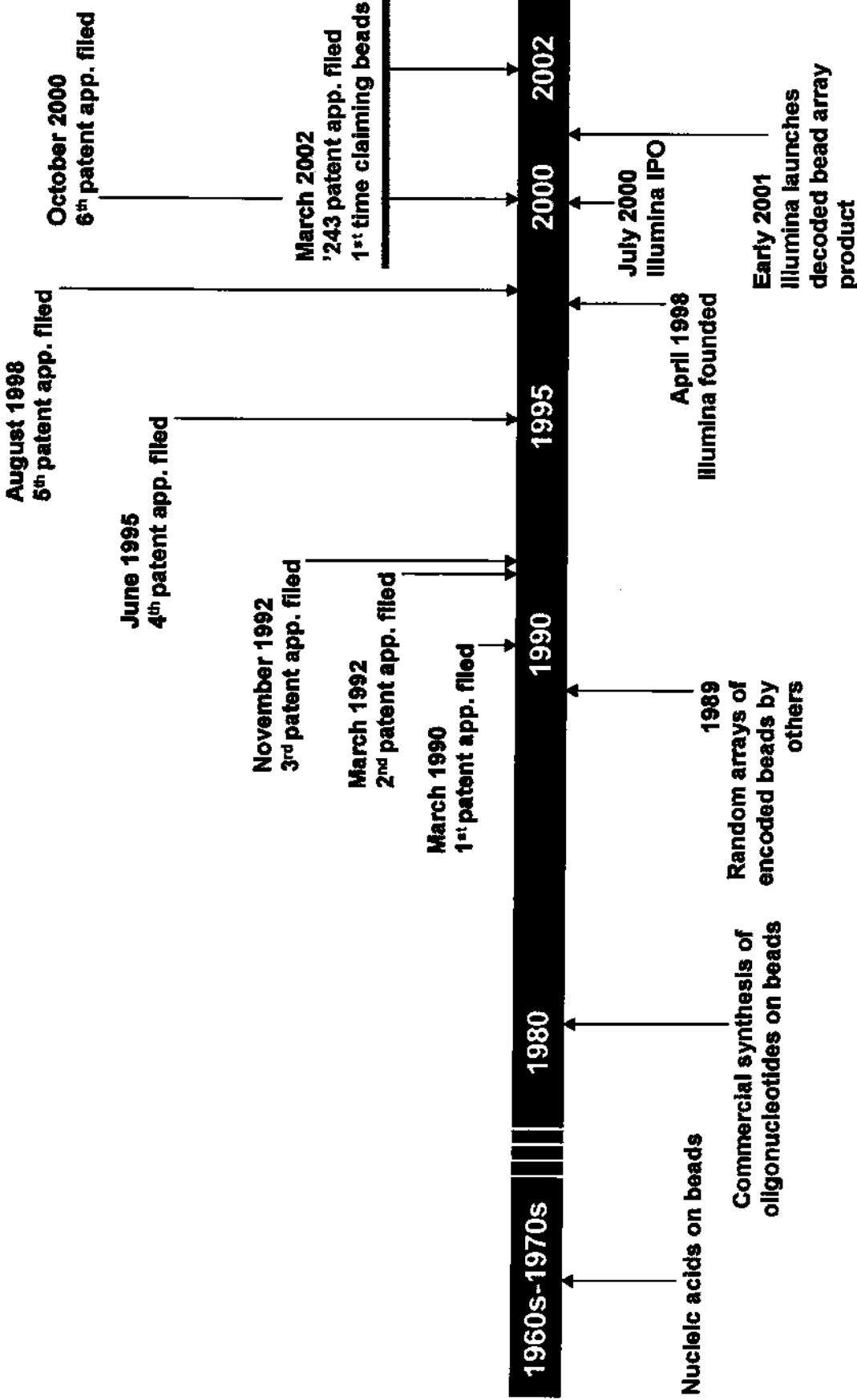
Illumina makes genotyping calls through transformation and clustering



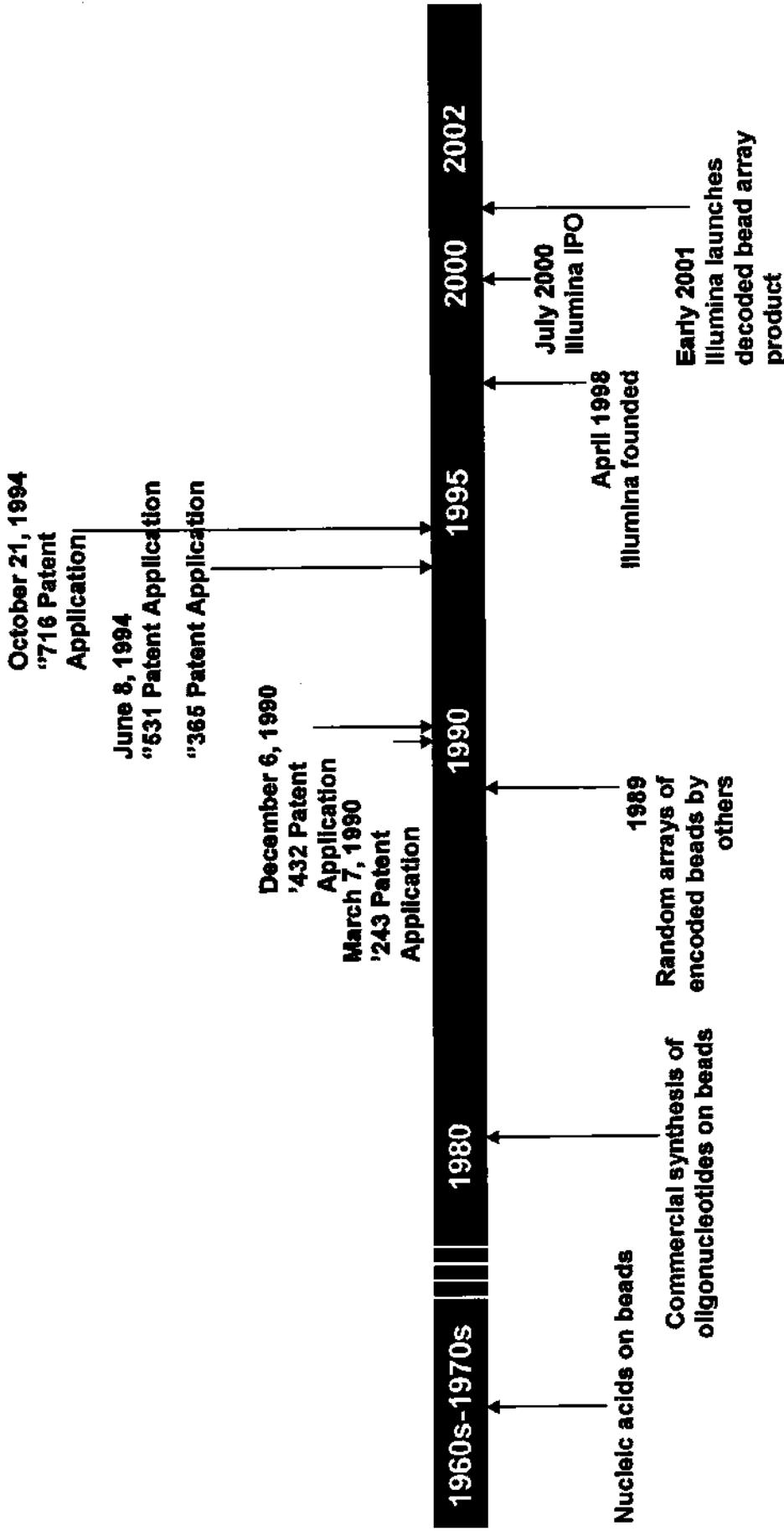
Illumina makes genotyping calls through transformation and clustering



Timeline of Applications Related to the '243 Patent



Timeline of Earliest Possible Filing of Affymetrix's Patents-In-Suit



Summary of Opinions

Evaluation of Patent Damages

- Reasonable royalties are appropriate

BeadArrays	4.5%	\$2,129,816
Instruments	2.0%	\$521,377
Services and research	3.0%	\$1,143,548
		\$3,794,742

(Through 2005)

Overview of Analysis

- Profit apportionment
- Design alternatives
- *Georgia-Pacific* factors

Reasonable Royalty

Overview of Analysis

- Profit apportionment
- Design alternatives
- *Georgia-Pacific* factors

Profit Apportionment

Illumina's Profits Are Attributable to Many Factors

- Illumina's research and development
- Manufacturing processes and efficiencies
- Marketing, sales and distribution expertise
- Brand and reputation
- Other patented technology

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Illumina's Profits Are Attributable to Many Factors

- Illumina's research and development
- Manufacturing processes and efficiencies
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- Brand and reputation
- **Other patented technology**

Illumina's Patents

Table of Contents

- We completed the Covaris acquisition, which we believe provided us with a comprehensive approach to bead-based analysis for Diagnostics research and development and Next-Gen and Next-Gen sequencing technologies. We believe this complements our two portfolio of products and services. We believe the Covaris technology will be highly complementary to our two portfolio of products and services. We believe a new platform will be able to enhance our capabilities to service our existing customers and accelerate the development of additional technologies, products and services.
- We completed the development and launch of our InGenome whole-genome sequencing solution. This family of products offers a flexible Biochip design and high density architecture. InGenome Whole-Genome Sequencing products are based on our BroadArray technology and provide the industry's only 100% quality control, with an average 99.99% feature redundancy. The revolutionary InGenome array and corresponding Sainlife Sequencing allows large-scale interrogation of variation in the human genome.
- We have been applying Biochip

Intellectual Property

We have an extensive patent portfolio, including, as of February 1, 2006, ownership of, or exclusive licenses to, 38 issued U.S. patents and 102 pending U.S. patent applications, including six allowed applications that have not yet issued as patents, some of which derive from a common parent application. Our issued patents, which cover various aspects of our array, assay, oligo synthesis, instrument and chemical detection technologies, expire between 2011 and 2022.

On those pages, all or some was added in later years, when no opportunity was recognized in revenue during the first quarter of fiscal 2006

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Attachment 1, Illumina
C.A. on file with J.P.
Trial Exhibit
DX 1516

Profit Apportionment

Tufts

- Worldwide, exclusive license
- Licenses patented technology underlying Illumina's accused products
- 3% royalty on net sales of beadarrays

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1. **Principles** - The **principles** of design and mechanics in order that strength
1. and safety may be obtained in the structure.

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12. Federal, state, and local governments and other organizations that have been involved in the development of such a program for the benefit of the public.

وَمَنْ يَعْمَلْ مِنْ حَسْنَاتِهِ فَلَا يُؤْمِنُ بِهَا وَمَنْ يَعْمَلْ مِنْ سُوءِهِ فَلَا يُؤْمِنُ بِهِ وَلَهُ عِلْمٌ بِمَا يَعْمَلُ

DN 1540

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Reasonable Royalty

Overview of Analysis

- Profit apportionment
- **Design alternatives**
- *Georgia-Pacific* factors

Design Alternatives

Overview

- Represents a cap as to what Illumina would be willing to pay for license
- Total cost to Illumina to implement is less than \$7 million

Design Alternatives

‘716 Patent

- No conversion step (Cartesian coordinates)
 - 2002 cost is \$75,000

OR

- Eliminate base call reporting
 - Minimal expense because commercially used previously

Design Alternatives

‘531 Patent

- One array per solid support
 - 2002 cost is several million dollars

Design Alternatives

‘365 Patent

- Non-barcode identification system
 - 2002 cost is less than \$0.5 million

Design Alternatives

'243 Patent

- White light with filters
 - 2002 cost is less than \$3 million

OR

- Nanocrystals

OR

- Non-covalent attachment
 - 2002 cost is less than \$0.5 million

Overview of Analysis

- Profit apportionment
- Design alternatives
- **Georgia-Pacific factors**

Licenses to Comparable Patents

PHRI

- Worldwide license
- Licenses patented array technology comparable at least to the '531 patent
- 0.7% royalty rate

<p>LICENSE AGREEMENT</p> <p>This Agreement, effective on the date first executed by us at the institutions herein, is between the Public Health Research Institute of the City of New York, Inc., a not-for-profit corporation of the State of New York having its principal place of business at 455 First Avenue, New York, NY 10016 (hereinafter "PHRI"), a corporation of the State of California having offices at 3380 Central Parkway, Santa Clara, CA 95051 ("Affymetrix"), collectively "The Parties."</p> <p>WHEREAS</p> <p>A. The name patent application relating to experimental chip arrays and methods employing such arrays, as hereinafter defined</p> <p>B. Affymetrix has developed, manufacturing and selling chips that include arrays of bound oligonucleotides and RNA complementary such chips.</p> <p>C. Affymetrix desires a worldwide exclusive license under said patent application and patent issuing therefrom</p> <p>D. That name patent application relating to labeled oligonucleotides referred to by PHRI as "molecular beacons" and to assays and kits employing said molecular beacon and to certain thionaphthalene probes for oligonucleotide probes.</p> <p>4/10/01 7/17/01 Affymetrix PHRI DX 772</p> <p>RIGHTS CONFIDENTIAL ATTORNEY'S EYES ONLY</p>	
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Affymetrix Changed The Algorithm For Its Genotyping Product

Algorithm and Blues: New Software Enables Affy to Cut 500K Price Tag, But Investors... Page 2 of 2

"Affy's management does a great job," says Michael J. Sullivane, a BMO Capital Markets analyst. "We feel very comfortable with the position and the pricing of those products. We don't see any direct impact."

According to Schiffman, Affy's original algorithm "only ran on the power of the server to do the calculations and to generate the raw data and then we had to take that raw data and then plug it up to their specific product." The added time the new algorithm would be in the hands of Affy's customers "was a manufacturing problem that affected the company to run on a 120/200 genome and a 100K genome and a 50K genome and a 25K genome with resultant time that resulted in the customers not being able to get their product out in time for their customers which, in turn, affected the timing of reorders."

"When they obtained software [there was a] larger degree of disparity between heterozygote calls and homozygote calls," Schiffman told the investors. "The new software algorithm takes the same information from the chip that we've already processed but provides them to extract all the information off the chip. It really has corrected the challenge we've seen in terms of the software." He said

Schiffman pointed out in May that the problems with the company's initial algorithm had created scale-up issues for Affy customers which, in turn, affected the timing of reorders. "[With the older software] there was a larger degree of disparity between heterozygote calls and homozygote calls," Schiffman told the investors.

<http://www.biostatnews.com/affy/14202-1.html#type1>

"They said, 'We don't see any direct impact.'

But that was not publicly disclosed as a motive for reducing a 1 million

Affymetrix / Home
CA Home
Tech Support
DX 1559

Source: "Algorithm And Blues New Software Enables Affy to Cut 500K Price Tag, But Investors Left Spooked," BioArray News (July 25, 2006)

Summary**Reasonable Royalties**

	Rate	Royalty Base	Royalties
BeadArrays	4.5%	\$47,329,254	\$2,129,816
Instruments	2.0%	\$26,068,872	\$521,377
Services and research	3.0%	\$38,118,264	\$1,143,548
\$3,794,742			(Through 2005)

Lost Profits Is Not Appropriate

Availability of Design Alternatives

- Illumina had design alternatives available
- Competitive technologies exist for which Dr. Lynde does not properly account

Capacity Constraints

SUSAN E. SIEGEL
Highly Confidential - Attorneys' Eyes Only
March 3, 2006

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At 1966, there was some latency, and when we introduced some of those, but then we had so much capacity because as a board we said we would always take ports capacity as we never be in those ratios and using capacity constraints, so although we'd have yield losses, we always had a lot of capacity. That wasn't the case in the second half.

So although

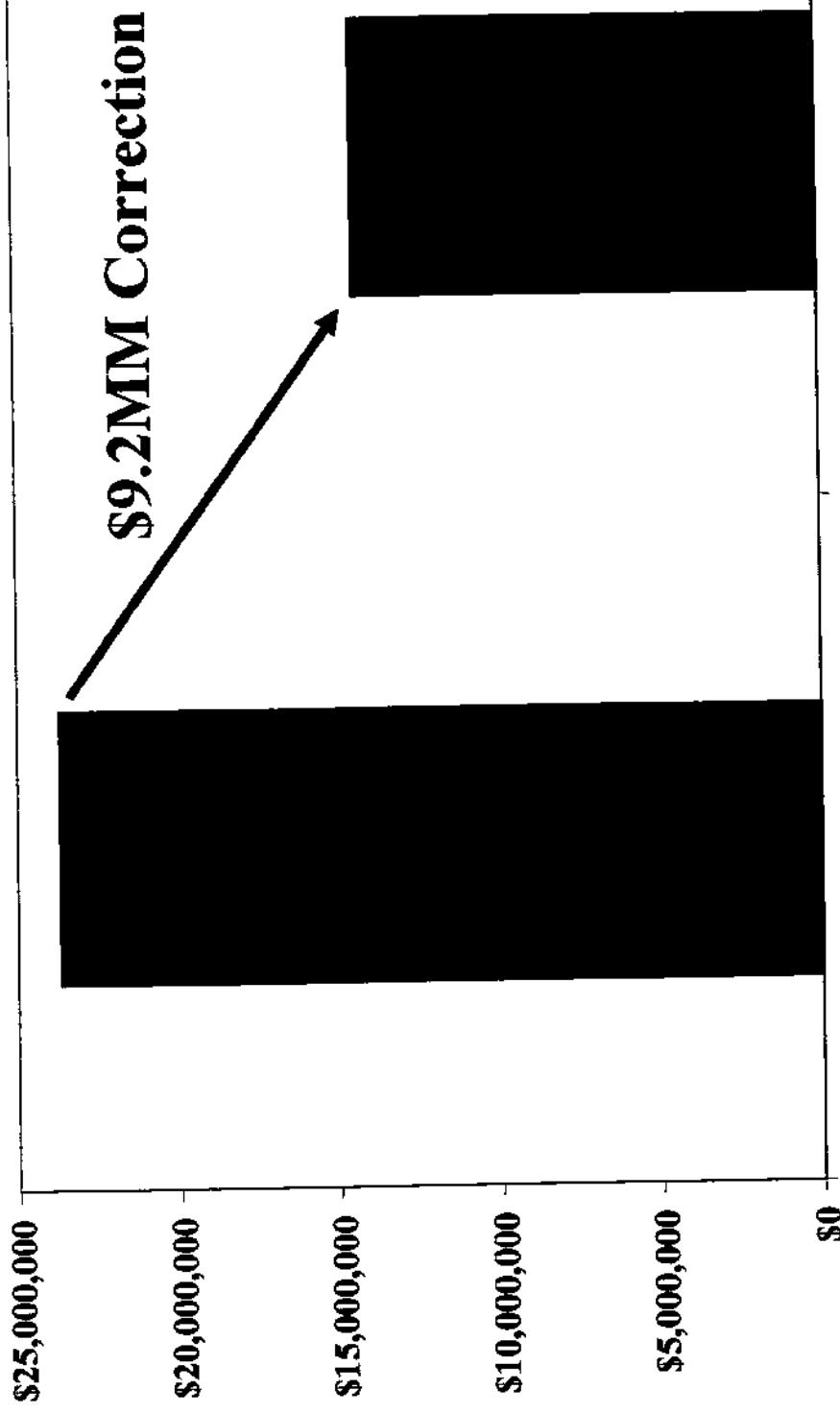
we'd have yield issues, we always had a lot of capacity. That wasn't the case in the second half of 2005.

21 THE VIDEO OPERATOR: Back on the record.
22
23 HP. COMPLAINT: Ms. Siegel, thank you very
24 The time is 4:46 PM.
25

Source: Siegel Dep., at 150:5-8

Overstates Lost Profits

Correcting for Capacity Constraints

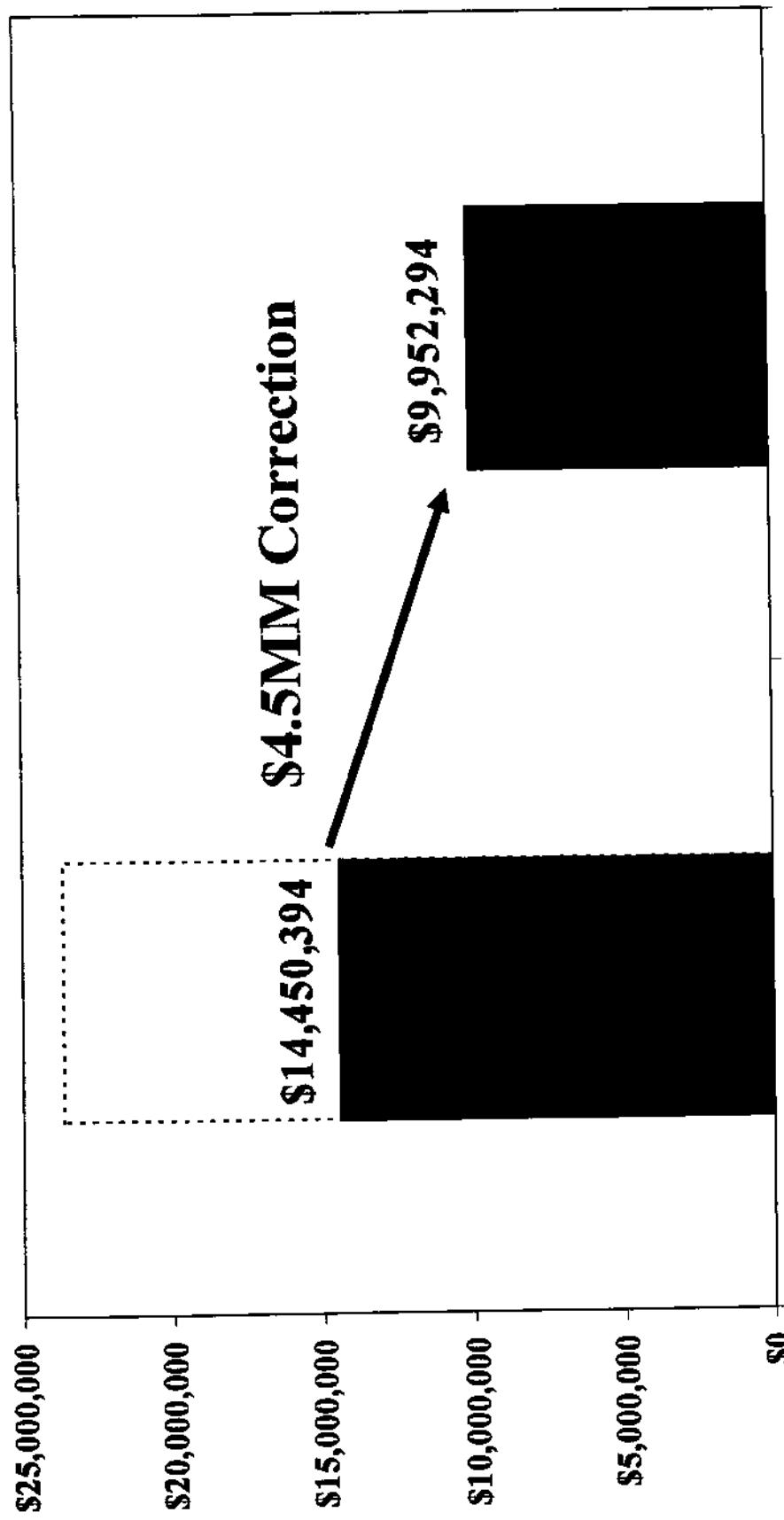


Dr. Lynde's Lost Profits

Dr. Lynde's Lost Profits Corrected for
Capacity Constraints

Overstates Lost Profits

Correcting for Lost Profits Claim for Instruments

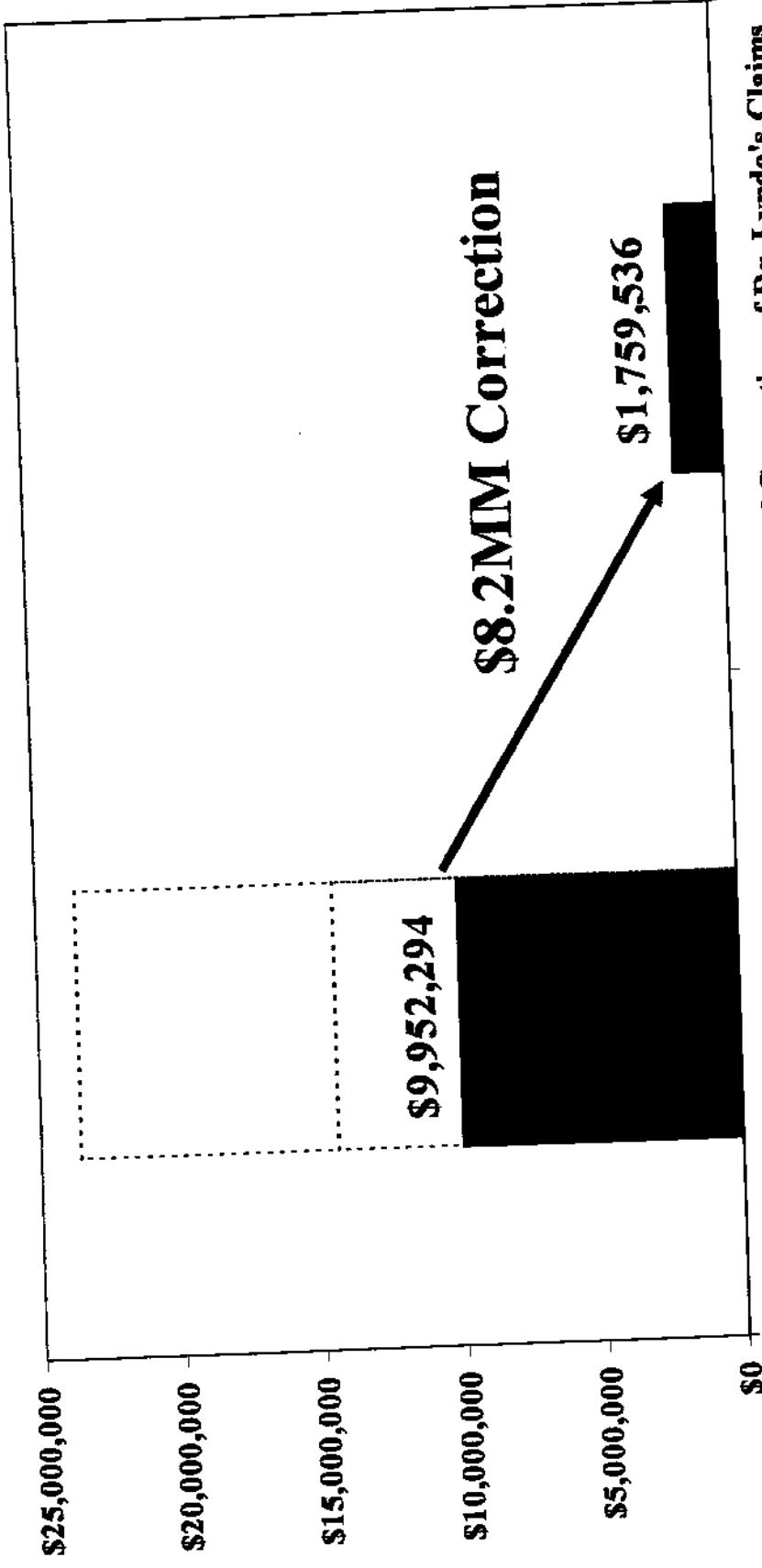


Dr. Lynde's Lost Profits Corrected for
Capacity Constraints

Additional Correction for Claim of Lost
Profits on Instruments

Overstates Lost Profits

Correcting for Lost Profits Claim For Incorrect Identification of Competitive Products

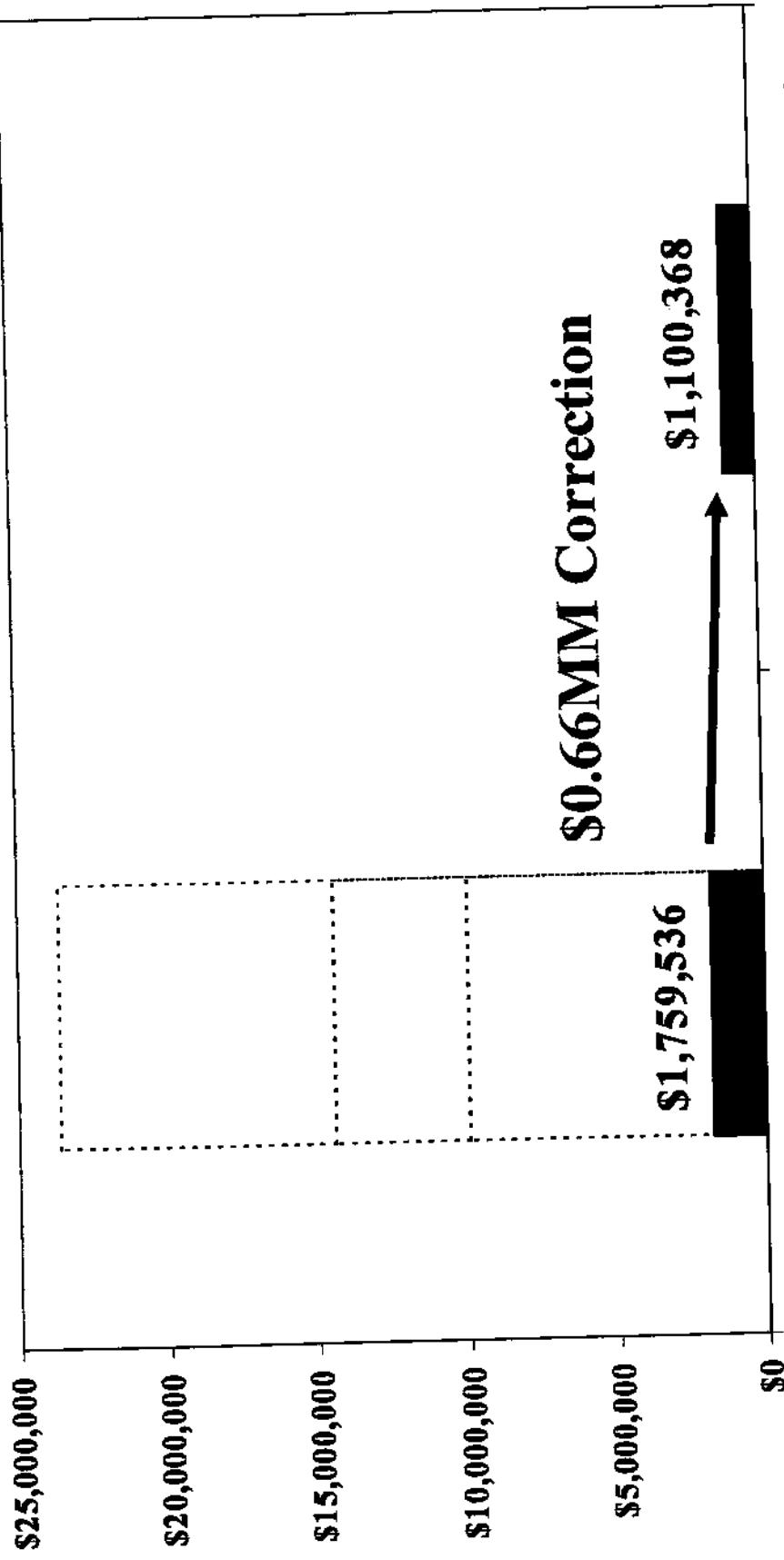


Dr. Lynde's Lost Profits Corrected for Capacity Constraints, Lost Profits on Instruments

Additional Correction of Dr. Lynde's Claims

Oversates Lost Profits

Correcting Dr. Lynde's Incremental Margin



Dr. Lynde's Lost Profits Corrected for
Capacity Constraints, Lost Profits on
Instruments, Adjusted Products

Additional Correction for Dr. Lynde's
Incremental Margins

Overstates Lost Profits

Lost Profits Summary

- If lost profits are appropriate, corrections to Dr. Lynde's lost profits calculation are necessary
- Correcting for these errors reduces Dr. Lynde's lost profits claim by **\$22,575,632** through 2005
- Dr. Lynde's lost profits claim should be adjusted to be no more than **\$1,100,368** through 2005

Takara-Shuzo Sought to Renegotiate

THEKKA
101, 17th Main 13th Cross Main, 977-312 2018
TANAKA SHIBU CO., LTD.
8-10, TAKAHASHI 1-chome, Tsurumi-ku, Yokohama 222-0033
TEL: 045-332-0001 FAX: 045-332-0002
E-mail: tanakashibu@tanakashibu.co.jp

Given the deleterious impact that the activities of Agilent and others have had on Takara Bio's market for the past half-year or more, we do not believe that we should have an obligation to make the minimum royalty payments until such time as the activities of all non-licensees have ceased and we are able to engage in the sale of microarray products under the fair market conditions contemplated by the License Agreement.

in the role of university professor within the faculty configuration recommended by the Curious Department. Until such time, we do not feel that we will be responsible for the outcomes of the Curious Department, except within the purview of the exhibition of our responsibilities. Based on the discussions we had to determine just what we do in service to within the university, namely, Professors 101 and 102, Professors 200 and 201, and so on. We are not in a position to do the activities of all the Curious have certain responsibilities.

found in Table 3 and Table 2 of article 4.2 of the Islamic agreement, and based on the same, without any replacement above, we believe the both this and reasonable sum (b) the reasonable part of the title that he holds in the Islamic agreement and article 4.2 with respect to using an ownership whose property have been held in his registered

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Oversates Reasonable Royalty Damages

Genomic Solutions

- Does not license any of the patents-in-suit
- Licenses 155 other Affymetrix patents and patent applications
- Genomic Solutions sought to renegotiate the terms to reduce the financial burden

Genomic Solutions Sought to Renegotiate

market pricing has deteriorated to the point that the current license terms.

it will be impossible to recover our investment in date under the current license terms.

In addition to the normal focus, we have recently been involved by Oxford Glass Technologies (a United of York Entrepreneur partner) in a project to assess the impact of the DGTI intellectual property

On May 29, 2007, the Board of Directors of the Company approved a resolution to increase the authorized capital of the Company by 100,000,000 shares of common stock.

Percentage of Open-Map States
that are utilized to map to Automap. 50% of the errors result in either closed codes and in non-geocoded credit codes

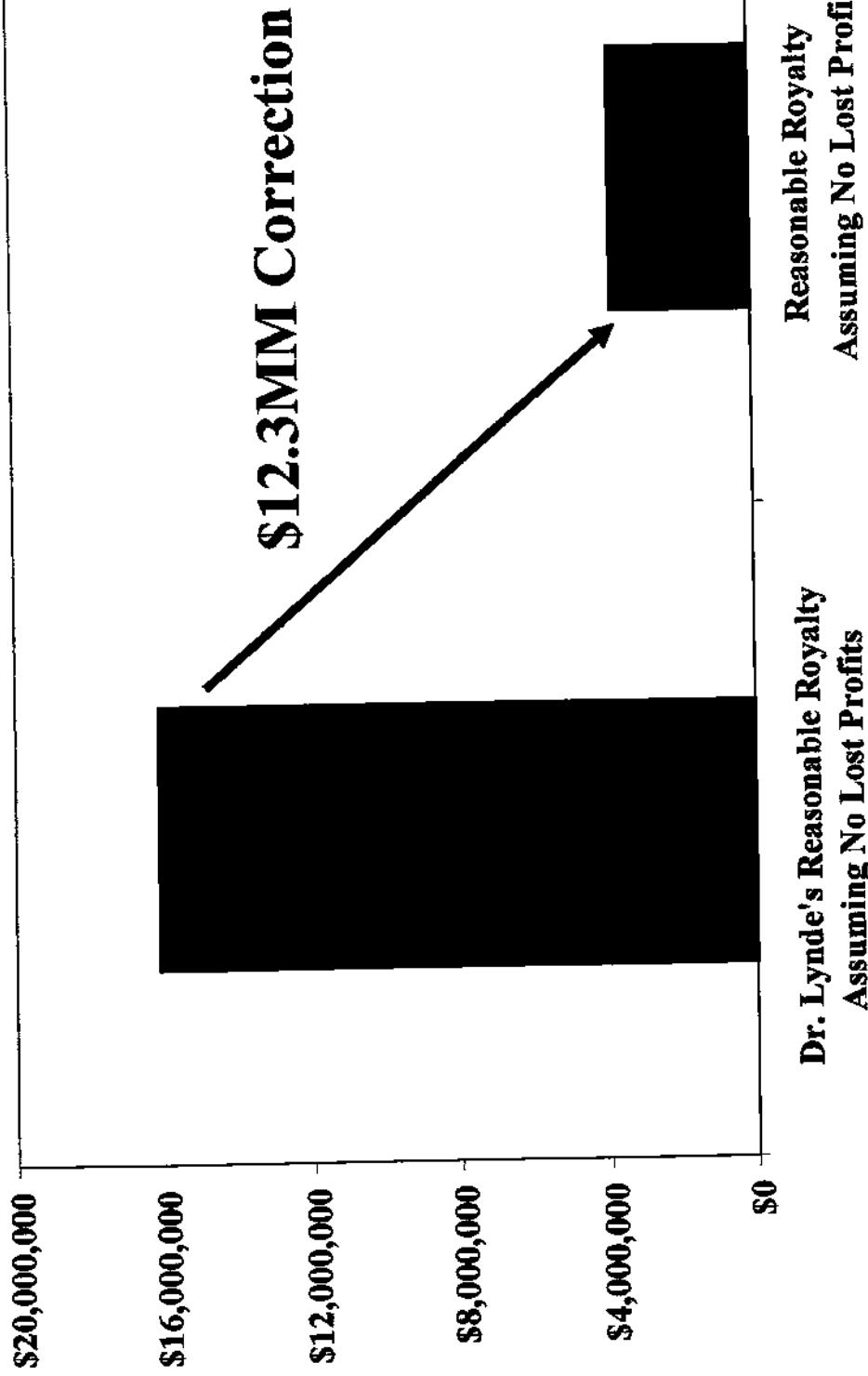
प्राचीन भूमिका व विवरण 11

W. S. Foy, Jr., Plaintiff
C. A. No. 1401-77
Trial庭
DX 1038

Highly Confidential - Attorneys' Eyes Only

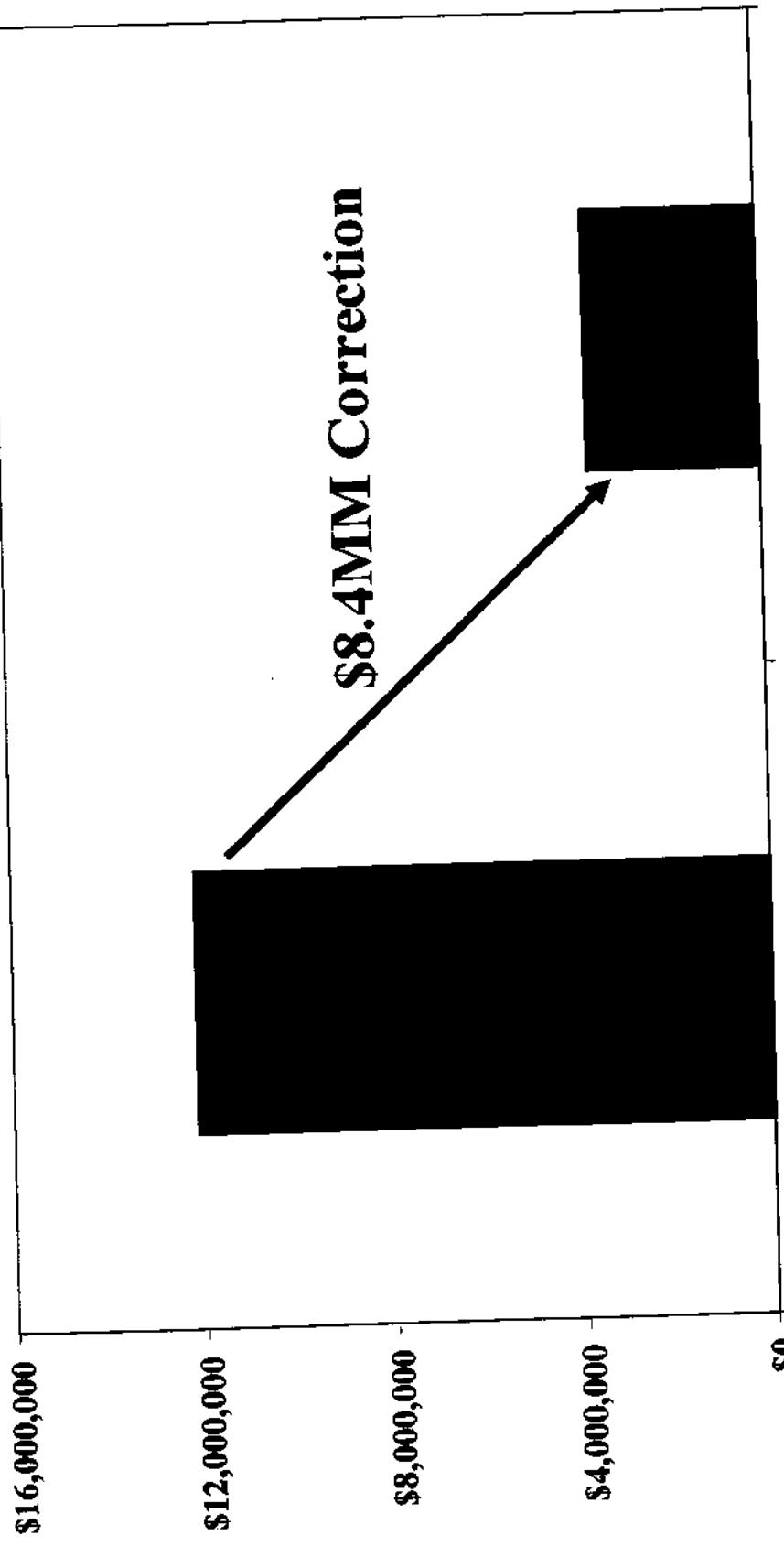
Overstates Reasonable Royalties

Reasonable Royalty Assuming No Lost Profits Award



Overslates Reasonable Royalties

Reasonable Royalty Assuming Lost Profits Award



Reasonable Royalty
Assuming Lost Profits Award
Dr. Lynde's Reasonable Royalty
Assuming Lost Profits Award

Summary of Opinions**Evaluation of Patent Damages**

	Rate	Royalties
BeadArrays	4.5%	\$2,129,816
Instruments	2.0%	\$521,377
Services and research	3.0%	\$1,143,548
\$3,794,742		

(Through 2005)